

In the Claims:

This listing of claims will replace all prior versions and listings of the claims in this application.

Listing of Claims

1. (Currently Amended) A purified and isolated non-naturally occurring nucleic acid ligand to a fibrillar protein target, wherein said ligand is an RNA ligand selected from the group ~~comprising~~ consisting of:

- (i) the nucleic acid depicted in any one of SEQ ID NOS: 1-55 or 58 –105;
- (ii) having the corresponding DNA or RNA sequences of any one of SEQ ID NOS: 1-55 or 58–105 or the corresponding fully complementary sequences thereof or their L-ribose derivatives; and
- (iii) derivatives of the sequence depicted in any one of SEQ ID NOS: 1-55 or 58 –105 having at least about 60%, 70%, 80% or 90% sequence identity to any one of the nucleotide sequences, and which have a binding affinity to a fibrillar protein.

2. (Currently Amended) The nucleic acid ligand according to claim 1 which is substantially homologous to and has substantially the same ability to bind said fibrillar protein target as a ligand ~~selected from the group comprising~~ the nucleic acids depicted in any one of SEQ ID NOS: 1-55 or 58 –105.

3. (Currently Amended) The nucleic acid ligand according to ~~either preceding claim which~~ claim 1, wherein the nucleic acid has substantially the same structure and the same ability to bind said fibrillar protein target as a ligand selected from the group comprising the nucleic acids depicted in any one of SEQ ID NOS: 1-55 or 58 –105.

4. (Currently Amended) The nucleic acid according to ~~any preceding claim~~ claim 1 wherein the fibrillar protein target is selected from the group ~~comprising~~ consisting of monomeric β 2m or A β 1-40 or A β 1-42, protofibrillar β 2m or A β 1-40 or A β 1-42[[,]] and mature fibrillar β 2m or

A β 1-40 or A β 1-42.

5. (Currently Amended) The nucleic acid according to ~~any preceding~~ claim 1 wherein the fibrillar protein target comprises either L- or D-amino acid molecules.

6. (Currently Amended) The nucleic acid according to ~~any preceding~~ claim 1 wherein the nucleic acid of any one of SEQ ID NOS: 1 to 16 ~~have a preferential~~ has a binding affinity to a D-amino acid A β 1-40 monomeric target.

7. (Currently Amended) The nucleic acid according to ~~any one of claims 1 to 5~~ claim 1 wherein the nucleic acid of any one of SEQ ID NOS: 17 to 36 ~~have a preferential~~ has a binding affinity to a D-amino acid A β 1-40 pre-fibrillar target.

8. (Currently Amended) The nucleic acid according to ~~any one of claims 1 to 5~~ claim 1 wherein the nucleic acid of any one of SEQ ID NOS: 37 to 55 ~~have a preferential~~ has a binding affinity to a D-amino acid A β 1-40 protofibril target.

9. (Currently Amended) The nucleic acid according to ~~any one of claims 1 to 5~~ claim 1 wherein the nucleic acid of any one SEQ ID NOS: 58 to 71 ~~have a preferential~~ has a binding affinity to a native β 2-microglobulin protein target.

10. (Currently Amended) The nucleic acid according to ~~any one of claims 1 to 5~~ claim 1 wherein the nucleic acid of any one of SEQ ID NOS: 72 to 90 ~~have a preferential~~ has a binding affinity to a β 2-microglobulin immature fibril protein target.

11. (Currently Amended) The nucleic acid according to ~~any one of claims 1 to 5~~ claim 1 wherein the nucleic acid of any one of SEQ ID NOS: 91 to 105 ~~have a preferential~~ has a binding affinity to a β 2-microglobulin mature fibrillar protein target.

12. (Currently Amended) The nucleic acid according to ~~any preceding claim~~ claim 1 further ~~including~~ comprising any one or more of the following features:

- (i) a fluorescent label;
- (ii) an imaging label ~~or~~; and
- (iii) a flanking region.

13. (Currently Amended) The nucleic acid according to claim 12 wherein the flanking region comprises any one or more nucleic acid sequences selected from the group ~~comprising~~ consisting of SEQ ID NOS: 56, 57, 106 and 107.

14. (Currently Amended) A vector comprising at least one or more nucleic acids ~~as defined in any preceding claim~~ of claim 1.

15. (Currently Amended) A host cell ~~including~~ comprising at least one or more nucleic acids ~~as defined in any of claims 1 to 13~~ claim 1 or ~~the vector of claim 14~~ a vector comprising the at least one or more nucleic acids of claim 1.

16. (Original) Use of a binding motif comprising a peptide sequence derived from human $\beta 2m$ that retains the ability of the whole protein to form amyloid fibrils, as a target for selecting a nucleic acid ligand.

17. (Original) Use of a peptide sequence comprising any one of SEQ ID NO: 111, 112 or 113 or derivatives or variants thereof that retain the ability of the whole protein to form amyloid fibrils, as a target for selecting a nucleic acid ligand.

18. (Currently Amended) A purified and isolated non-naturally occurring nucleic acid ligand to a fibrillar protein target, wherein the target comprises a the binding motif of ~~as defined in either claim 16 or 17~~.

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19. (Original) A purified and isolated non-naturally occurring nucleic acid ligand to a fibril cross β -core protein target.

20. (Currently Amended) A pharmaceutical composition comprising at least one nucleic acid ~~as defined in any one of claims 1 to 13 of claim 1 or the vector of claim 14 or the vector comprising the at least one or more nucleic acids of claim 1~~ .

21. (Currently Amended) A pharmaceutical composition according to claim 20 comprising a ~~number of at least two~~ nucleic acid ligands each with binding affinities for the same or different forms of a fibrillar protein.

22. (Currently Amended) A pharmaceutical according to ~~either~~ claim 20 ~~or 21~~ further ~~including~~ comprising a suitable excipient, diluent or carrier.

23. (Currently Amended) Use of a nucleic acid according to ~~any one of claims 1 to 13~~ claim 1 for the manufacture of a medicament for treating amyloid diseases.

24. (Original) Use according to claim 23 for the treatment of Alzheimer's and DRA disease conditions.

25. (Currently Amended) A method of treating a patient suffering from Alzheimer's disease or a disease associated with amyloid formation comprising administering a therapeutically effective amount of a (i) the nucleic acid ligand according to any one of claims 1 to 13 claim 1, the vector of claim 14 or a pharmaceutical according to claims 20 to 22 (ii) a vector comprising the nucleic acids of claim 1, or (iii) a pharmaceutical composition comprising (i) or (ii).

26. (Currently Amended) A method according to claim 25 wherein the therapeutically effective amount of a nucleic acid ligand, ~~or~~ vector or pharmaceutical composition is administered by an intra-venous, intra-muscular, intra-peritoneal route and optionally is

administered on more than one occasion.

27. (Currently Amended) Use of the nucleic acid according to ~~any one of claims 1 to 13~~ claim 1 or the vector of claim 14 a vector comprising the nucleic acids of claim 1 as a diagnostic agent for detecting the presence and/or progression of an amyloid disease.

28. (Currently Amended) A method of monitoring the presence and/or progression of an amyloid disease comprising:

(a) administering to a patient at least one nucleic acid according to any one of claims 1 to 13 or the vector of claim 14 or a pharmaceutical according to any one of claims 20 to 22 (i) the nucleic acid ligand according to claim 1, (ii) a vector comprising the nucleic acids of claim 1, or (iii) a pharmaceutical composition comprising (i) or (ii);

(b) imaging the presence of binding of said nucleic acid ligand to an amyloid fibril; and

(c) optionally repeating the process at a later date to assess presence or progression of a disease state.

29. (Original) A method for the isolation of nucleic acid ligands to a fibrillar protein target comprising:

- (i) preparing a candidate mixture of nucleic acids;
- (ii) contacting the candidate mixture of nucleic acids with a biotinylated immobilised fibrillar protein on ice, wherein nucleic acids having an increased affinity to the fibrillar protein relative to the candidate mixture are partitioned from the remainder of the candidate mixture;
- (iii) partitioning the increased-affinity nucleic acids from the remainder of the candidate mixture;
- (iv) amplifying the increased-affinity nucleic acids to yield a mixture of nucleic acids with relatively high affinity and specificity for binding to the fibrillar protein, whereby a nucleic acid ligand of the fibrillar protein may be identified.

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30. (Original) A method according to claim 29 wherein the candidate mixture comprises single stranded nucleic acids.

31. (Original) A method according to claim 30 wherein the single stranded nucleic acids comprise ribonucleic acids.

32. (Currently Amended) ~~[[A]] The method according to any one of claims 29 to 31~~ claim 29 further ~~including the step of comprising~~ modifying the nucleic acid ligand with a fluorescent label and/or an imaging reagent.

33. (Currently Amended) A method according to ~~any one of claims 29 to 32~~ claim 29 wherein the nucleic acid ligand further comprises a flanking selected from the group ~~comprising~~ consisting of SEQ ID NO: 56, 57, 107 ~~or~~ and 108.

34. (Currently Amended) A nucleic acid product identified and isolated according to the method of ~~any one of claims 29 to 33~~ claim 29.